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(19)(CA) **CANADIAN PATENT** (12)

(54) Long-Active Drug Formulations Comprising Galanthamine for Treatment of Alzheimer's Disease

(72) Davis, Bonnie , U.S.A.
Goodman, Morris , Canada

(73) Davis, Bonnie , U.S.A.
Goodman, Morris , Canada

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NO DRAWING

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A B S T R A C T

Long-acting Galanthamine formulation is prepared by coating particles of drug with polyvinyl pyrrolidone, sizing the particles and incorporating them into a capsule or tablet.

The present invention relates to long-acting formulations for treatment of Alzheimer's disease and related dementias.

United States Patent No. 4,663,318 (Davis issued May 5, 1987) describes the use of galanthamine and its salts for treatment of Alzheimer's disease and related dementias. The possibility of using a long-acting formulation of the drug is suggested therein.

According to the present invention, there is provided a sustained release formulation in the form of a tablet or capsule for oral administration for treatment of Alzheimer's disease and related dementias comprising particles of galanthamine or a pharmaceutically acceptable salt thereof.

A preferred compound of the above formula is galanthamine hydrobromide.

Suitable pharmaceutically acceptable coating agents include polyvinyl pyrrolidone.

A particularly useful method for producing formulations of the present invention is to coat the drug substance with polyvinyl pyrrolidone alcohol solution to form granules. These granules are then passed thru a sieve machine to obtain various sizes of granules. A determined amount of each of different size granules are mixed with excipient such as hydroxypropyl methyl cellulose, ethyl cellulose, starch, silicon dioxide, and with a lubricant such as magnesium stearate or polyethylene glycol to form a tablet or to be incorporated into a capsule.

The final drug preparation is tested for dissolution profile in addition to the general testing requirements. A useful dissolution profile for a sustained release preparation according to the present invention is:

Active drug	1-2 hours	10-20%
dissolved	2-4 hours	20-40%
in gastric	4-8 hours	40-80%
juice	12 hours	balance

Typically the sizing of the particles incorporated into a table or capsule will be chosen so as to produce a sustained release over a four to twelve hour period, for example, over a eight hour period.

Typically capsules or tablets according to the present invention contain a quarter to a half of the typical daily dose of drug, although dosage units outside this range are also possible. Such daily doses are normally for 10 to 2000 mg per day, more typically 100 to 600 mg per day. Typically, therefore, tablets or capsules comprise 25 to 250 mg of active compound.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE

3 CLAIMED ARE DEFINED AS FOLLOWS:

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1. A sustained release formulation for oral administration in the form of a tablet or capsule for treatment of Alzheimer's disease and related dementias comprising particles of galanthamine or a pharmaceutically acceptable salt thereof, said particles being coated with a pharmaceutically acceptable coating agent that is soluble in the intestinal tract, the thickness of the coatings varying between individual particles, a plurality of said particles having various coating thickness chosen so as to result, after administration, in release of the drug from its coated particles at different times.

2. A sustained release formulation as claimed in claim 1 wherein said particles comprise galanthamine hydrobromide.

3. A sustained release formulation as claimed in claim 1 wherein said coating material is polyvinyl pyrrolidone.

4. A sustained release formulation as claimed in claim 1 containing 25 to 250 mg of active compound.

SUBSTITUTE

REMPLACEMENT

SECTION is not Present

Cette Section est Absente